

APPENDIX 8

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
WESTERN DIVISION

J.B.D.L. Corp. d/b/a
BECKETT APOTHECARY, et al.,

Plaintiffs,

Civil Action No.:

v.

C-1-01-704

WYETH-AYERST LABORATORIES, INC.,
et al.,

Defendants.

_____ /

DEPONENT: VERONICA T. MALLETT, M.D.

DATE: August 6, 2004

TIME: 9:00 a.m.

LOCATION: 20301 Oakwood Boulevard
Dearborn, Michigan 48124

APPEARANCES:

For the Direct Purchaser Class Plaintiffs:

MS. JAN BARTELLI

Garwin, Bronzaft, Gerstein & Fisher, L.L.P.

1501 Broadway

New York, New York 10036

(212) 398-0055

For the Direct Purchaser Class Plaintiffs:

MR. BRETT H. CEBULASH

Garwin, Bronzaft, Gerstein & Fisher, L.L.P.

1501 Broadway

New York, New York 10036

(212) 398-0055

<p style="text-align: right;">Page 70</p> <p>1 Q You can answer the question.</p> <p>2 A I -- my assessment is that the point the authors are trying</p> <p>3 to make is that the coating is designed to absorb oxygen and</p> <p>4 prevent oxidation, and that a -- an additional benefit of</p> <p>5 that, the purpose of that, while also avoiding oxidation of</p> <p>6 the constituent estrogens, it also prevents the escape of</p> <p>7 odor, according to the authors.</p> <p>8 Q What odor do you think is being referred to here?</p> <p>9 MR. EGGERT: Well, objection as to how on earth she</p> <p>10 would know what odor the authors Hess, Pharm and Schwartz</p> <p>11 might have had in mind.</p> <p>12 BY MS. BARTELLI, CONTINUING:</p> <p>13 Q You can answer the question.</p> <p>14 A I truly could not tell you. But I would understand that</p> <p>15 since the primary content of the drug is estrogen, it would</p> <p>16 be the odor of estrogen.</p> <p>17 Q Are you aware of any other estrogen tablets that use shellac</p> <p>18 as their coating?</p> <p>19 A No. I'm also not aware of the coating of any other estrogen</p> <p>20 tablets.</p> <p>21 Q Have you ever smelled estrogen from any other estrogen</p> <p>22 product that you've used?</p> <p>23 A No.</p> <p>24 Q So it wouldn't appear that other estrogen products need to be</p> <p>25 coated with shellac to disguise the smell of estrogen?</p>	<p style="text-align: right;">Page 72</p> <p>1 Q So here the issue -- well, do you understand the issue to be</p> <p>2 that -- that the FDA is saying that an immediate release is</p> <p>3 less desirable than a slow release mechanism?</p> <p>4 A Right. That the Premarin tablet had a benefit by having the</p> <p>5 particular absorptive characteristics that it did, and having</p> <p>6 the shellac coating, and that made it a more slow release</p> <p>7 product. And this was actually a safer formulation than the</p> <p>8 generic estrogen tablet that -- that they discussed in that</p> <p>9 paragraph. They also said that the immediate release of</p> <p>10 estrogen causes higher blood level, estrogen levels and thus</p> <p>11 possible adverse effects such as breast tenderness. The risk</p> <p>12 of breast cancer, which was deemed to be dose related, might</p> <p>13 be increased compared to an estrogen formulation with a</p> <p>14 modified release dissolution profile such as Premarin.</p> <p>15 Q So the -- so your understanding then, the point being that if</p> <p>16 you have bursts or quick release of estrogen, that that is</p> <p>17 less desirable than a slow release?</p> <p>18 A It would appear so from this author's compilation of the --</p> <p>19 the data.</p> <p>20 Q Do you agree with that statement, based on your own</p> <p>21 experience?</p> <p>22 A I really don't have personal experience which to -- to say,</p> <p>23 I -- okay. Ask me that question again.</p> <p>24 Q Do you agree with the statement regarding immediate release</p> <p>25 mechanisms versus slow release mechanisms in terms of benefit</p>
<p style="text-align: right;">Page 71</p> <p>1 A Well, as I stated previously, I thought the shellac was used</p> <p>2 to prevent oxidation. And I truly don't know what odor</p> <p>3 they're trying to disguise, if they are at all trying to</p> <p>4 disguise an odor.</p> <p>5 Q Now this article also discusses the issue of dissolution with</p> <p>6 Premarin and Cenestin products, does it not?</p> <p>7 A Yes.</p> <p>8 Q What is your understanding of the findings of this article?</p> <p>9 A That the dissolution testing of the conjugated equine</p> <p>10 estrogen as it was presented here appeared to function as a</p> <p>11 modified released agent. The paragraph under the subheading</p> <p>12 Dissolution Characteristics of Slow-Absorption CEE refers to</p> <p>13 this slow dissolution profile to be characteristic of the</p> <p>14 shellac coating of the Premarin tablet, particularly at</p> <p>15 acidic pH levels. It says in comparison to other generic</p> <p>16 estrogen products then available demonstrated immediate</p> <p>17 release dissolution profiles suggest the likelihood that</p> <p>18 there would be significant differences in blood level. The</p> <p>19 FDA found that these modified released characteristics of</p> <p>20 this CEE with the shellac coating was actually a -- a benefit</p> <p>21 of Premarin. And they concluded that while extended --</p> <p>22 extensive clinical data on the question was lacking, it</p> <p>23 appeared that high blood levels of estrogen resulting from</p> <p>24 immediate release products, those other than -- than</p> <p>25 Premarin, raised potentially significant safety issues.</p>	<p style="text-align: right;">Page 73</p> <p>1 or less benefit?</p> <p>2 A To -- yes. To -- to the degree that the references cited</p> <p>3 support that.</p> <p>4 Q Do you have any personal experience that would support that</p> <p>5 statement?</p> <p>6 A No, I don't.</p> <p>7 Q Can you turn to page 88.</p> <p>8 A Yes.</p> <p>9 Q If you look at the -- I guess it's the start of the second</p> <p>10 full paragraph.</p> <p>11 A Yes.</p> <p>12 Q And it's the -- first, second -- third sentence in that</p> <p>13 paragraph. Can you read that?</p> <p>14 A The --</p> <p>15 Q Where it starts however.</p> <p>16 A Second paragraph? Third sentence?</p> <p>17 Q It's the second full paragraph. The first word in the</p> <p>18 paragraph is accordingly.</p> <p>19 A Oh.</p> <p>20 Q And then it says accordingly, the FDA.</p> <p>21 A It says, however, in attempting to establish uniform in vitro</p> <p>22 dissolution characteristics of Premarin for purposes of</p> <p>23 bioequivalency comparisons, it was discovered that in fact</p> <p>24 CEE dissolved at an inconsistent rate varying widely, not</p> <p>25 only from batch to batch, but also between individual</p>

<p style="text-align: right;">Page 74</p> <p>1 tablets.</p> <p>2 Q And then the next --</p> <p>3 A Sentence?</p> <p>4 Q The next two, if you would.</p> <p>5 A This variability is likely due at least in part to the</p> <p>6 physical characteristics of the shellac coating applied to</p> <p>7 Premarin tablets. Over time, the protective shellac oxidizes</p> <p>8 and tends to crack, permitting older tablets to dissolve more</p> <p>9 rapidly.</p> <p>10 Q And then the next sentence reads, over the past 18 months</p> <p>11 alone, failure in dissolution testing has led to a number of</p> <p>12 large recalls now approaching a total of 500 million Premarin</p> <p>13 tablets. Do you see that?</p> <p>14 A Yes, I do.</p> <p>15 Q Now, does that indicate to you that at least in this author's</p> <p>16 opinion, that because of that coating, you -- Premarin in</p> <p>17 fact often has a problem with immediate or burst release of</p> <p>18 estrogen?</p> <p>19 MR. EGGERT: Objection, mischaracterization of the</p> <p>20 article.</p> <p>21 BY MS. BARTELLI, CONTINUING:</p> <p>22 Q You can answer.</p> <p>23 A It would indicate to me, but they don't provide any credible</p> <p>24 data to support that statement. The -- I think that is what</p> <p>25 the authors propose, but they don't provide any credible data</p>	<p style="text-align: right;">Page 76</p> <p>1 reader, have the option to endorse or believe in the message.</p> <p>2 But declaring that the product is -- the data is provided by</p> <p>3 the owner of the pharmaceutical company does at least give</p> <p>4 them the credibility of being up front about where the data</p> <p>5 came from.</p> <p>6 Q Aren't they required to do that?</p> <p>7 A Well, they're required to do that to the FDA. We're talking</p> <p>8 about in publications, are we not?</p> <p>9 Q Yes.</p> <p>10 A Oh. Okay. There's a difference.</p> <p>11 Q Right.</p> <p>12 A Right.</p> <p>13 Q So your position is that they're not -- a manufacturer is not</p> <p>14 required in a journal or scientific publication to disclose</p> <p>15 that they've somehow been involved in providing data or</p> <p>16 sponsoring?</p> <p>17 A Well, they didn't in this article. Most peer reviewed</p> <p>18 journals would require that. This is not, however, a peer</p> <p>19 reviewed journal, which also limits its credibility as a</p> <p>20 source.</p> <p>21 Q Do you think that the FDA is objective in the evaluations</p> <p>22 they do of particular drugs?</p> <p>23 A Yes. I think that they set standards and have guidelines for</p> <p>24 maintaining that -- the quality of drugs that enter into the</p> <p>25 U.S. drug supply. We hope so, anyway.</p>
<p style="text-align: right;">Page 75</p> <p>1 to support their position.</p> <p>2 Q And why do you say that?</p> <p>3 A The citation to support this comparison of bioequivalent is</p> <p>4 the data on file from the Duramed Pharmaceuticals which makes</p> <p>5 me suspect that the authors have a relationship with Duramed.</p> <p>6 Pharmaceutical companies are not in the habit of providing</p> <p>7 their data and to -- to test products objectively.</p> <p>8 Q So --</p> <p>9 A Of their competition.</p> <p>10 Q -- are you saying that when a pharmaceutical company provides</p> <p>11 data --</p> <p>12 A About a competitor's product.</p> <p>13 Q -- that it's --</p> <p>14 A That -- that -- the -- the possibility exists that -- that --</p> <p>15 that bias may have entered into the compiling of that data.</p> <p>16 Q So would it then be your position that if Wyeth had supplied</p> <p>17 data for an article that was somehow critical of Cenestin,</p> <p>18 that that bias also would exist?</p> <p>19 A If that was the only basis from which an author made a</p> <p>20 conclusion about a competitor's product, I would say that --</p> <p>21 that, yes, bias could exist.</p> <p>22 Q Is it your position that if a manufacturer provides data for</p> <p>23 an article that is supportive of their product, that bias</p> <p>24 also could exist?</p> <p>25 A I think that it is a possibility. Now, if that -- you, as a</p>	<p style="text-align: right;">Page 77</p> <p>1 Q Could you look at page 26 of your report.</p> <p>2 A Yes.</p> <p>3 Q Talking about the dissolution aspect.</p> <p>4 MR. EGGERT: Which paragraph are you referring to?</p> <p>5 THE WITNESS: Page 26?</p> <p>6 BY MS. BARTELLI, CONTINUING:</p> <p>7 Q I'm -- are you on page 26?</p> <p>8 A Yes.</p> <p>9 Q Okay. It's the middle of the paragraph which has continued</p> <p>10 from the previous page. And the sentence is nevertheless,</p> <p>11 the characteristics of the dissolution -- dissolution of an</p> <p>12 estrogen therapy play little role in my selection of hormonal</p> <p>13 agents.</p> <p>14 A Yes.</p> <p>15 Q I am not aware this has played any role in other physicians'</p> <p>16 selection of hormonal agents. And moreover, the fact that</p> <p>17 some Premarin tablets have been recalled due to manufacturing</p> <p>18 issues does not diminish the drug's safety or efficacy. Why</p> <p>19 do you think that the characteristics of dissolution of</p> <p>20 estrogen therapy is insignificant?</p> <p>21 A Well, because Premarin has been administered over an</p> <p>22 inordinately long period of time, and its efficacy has been</p> <p>23 well established and is not in doubt. And so characteristics</p> <p>24 of dissolution, if they were of question, don't have any</p> <p>25 clinical relevance.</p>